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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,626	07/24/2003	Steven P. Adams	14406-003005	9041

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FISH & RICHARDSON P.C.
1425 K STREET, N.W.
11TH FLOOR
WASHINGTON, DC 20005-3500

EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,626	ADAMS ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-15* is/are pending in the application.

4a) Of the above claim(s) *subject matter wherein Y is -CH2- or -SO2-* is/are withdrawn from consideration.

5)☒ Claim(s) *1-7 and 9-11, excluding non-elected subject matter* is/are allowed.

6)☒ Claim(s) *12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7 and 9-15 pending in the instant application.

Response to Amendment

1. Receipt is acknowledged of Applicants' Amendment and Response, submitted May 12, 2004, which has been reviewed by the Examiner and entered of record in the file. Accordingly, claim 8 has been cancelled, and claims 1, 9, 11, and 12 have been amended.

Election/Restrictions

2. Newly submitted subject matter of claims 1, 11, and 12, i.e. wherein Y is $-CH_2-$ or $-SO_2$, is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicants had originally directed the instant claims to the subject matter of Groups II and IV of the initial restriction requirement, i.e. compounds wherein X is –COOH, $-SO_2R_5-$, or $-SO_3H$, Y is –CO-, and R_1-R_4 have no carbocyclic aryl or heterocyclic groups.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, subject matter of claims 1, 11, and 12 wherein Y is $-CH_2-$ or $-SO_2-$ withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Applicant is advised that should they pursue the subject matter in question, the attached Klinger et al reference will be applied as 35 USC 102(b) art against claims 1-7 and 9-11, i.e. compounds according to formula (I), wherein Y is $-CH_2-$.

Response to Arguments

Claim Rejections - 35 USC § 112

4. The Examiner had previously rejected claims 12-15 under 35 USC 112, first paragraph, as not being enabled. Claim 12, now in amended form, still does not meet the requirements of 35 USC 112, first paragraph.

5. However, claims 12-14 newly rejected under 35 U.S.C. 112, first paragraph, as being reach-through claims. The claims are directed to a method of preventing, inhibiting, or suppressing cell adhesion in a mammal, yet these claims does not meet the requirements for "how to use" under 35 U.S.C. 112, first paragraph, and 35 U.S.C. 101, as stated below. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

6. Claim 12-15 previously rejected under 35 U.S.C. 112, first paragraph, as not reasonably providing enablement for preventing any and all of the cell-adhesion associated diseases encompassed by the claims. In response, Applicants have amended the claim to include the phrase "in need thereof," however, this only satisfies part of the requirements of 35 USC 112.

7. While said diseases may be listed on pages 37-38 of the specification, the "laundry list" of diseases and conditions encompassed by claims 12-15 is not enabled. Therefore, the Examiner maintains the rejection of the claims under 35 U.S.C. 112. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,

6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the aforementioned claims are directed to many diseases that are not enabled in the specification, including those recited in claim 15.

The nature of the invention

The nature of the invention is of methods of treating many different unrelated diseases or conditions, comprising administering the instant claimed compound to a patient in need thereof.

The state of the prior art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. Furthermore, the diseases recited within claims 14 and 15 are not the same but different diseases. By definition, autoimmune (for example rheumatoid arthritis, lupus erythematosus, and multiple sclerosis) refers to diseases against "self," while diseases such as psoriasis, diabetes, IBD and asthma are not encompassed by this definition and are completely unrelated. Such as all insulin-dependent diabetes mellitus patients require administering a hyperglycemic agent, on the other hand, treating autoimmune diseases employs the use of immunosupressants.

The predictability or lack thereof in the art

The immune response of a living organism is a complex, specific and interrelated process. It involves the overall coordination of all the lymphocytes, B-types, T-types, etc., their population, expression and interaction. The intertwined dependency and complexity in bio-feedback control relationships involves enormous biological pathways and physiological homeostasis.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of claim 1 and the inhibition of VLA4-mediated cell adhesion, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1.

The amount of direction or guidance present

The specification has enabled only the compounds according to claim 1 that selectively inhibit the binding of ligands to VLA-4. Furthermore, treatment of the claimed distinct diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating the symptoms of psoriasis (itchy, inflamed skin) would not employ the same methods as treating the symptoms of rheumatoid arthritis (stiffness and joint pain). The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

The presence or absence of working examples

The data provided in the disclosure on the inhibition of binding activity of ligands towards VLA-4 is insufficient evidence for methods of treating all claimed diseases. In fact, the only disclosure in the specification at all is found on pages 116-126 wherein two ELISA assays are described, and two animal examples are given (one which enables Applicants for treating

contact sensitivity in mice, the other for airway sensitivity in sheep). In view of the diversified multiple diseases as claimed, such few universal disclosures fails to provide specific description in guiding one skilled in the art to pick and choose the specific compounds that would be useful for treating one or a specific group of pathological conditions. The standard of 35 USC 112, first paragraph rejections is that the application *itself* must inform, rather than direct, others to find out for themselves, please see *In re Garnder*, 166 USPQ 138.

The breadth of the claims

Applicants are claiming methods of treating a broad number of diseases that are unrelated. The allegation that the diseases claimed by the Applicants are all treated by inhibiting the binding of ligands to VLA-4 is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the claimed diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every unrelated disease/condition encompassed by claims 12-15, using the instant claimed compounds. One of skill in the art would need to determine what listed diseases would be benefited by the stimulation of cannabinoid receptors and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the diseases by said stimulation.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine

which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of all claimed diseases. As a result, necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 12-14 rejected under 35 U.S.C. 101 as being reach-through claims, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claimed methods of preventing, inhibiting, or suppressing cell adhesion in a mammal do not comply with the utility requirement since there is no disclosed pharmaceutical use, i.e. a method of "preventing, inhibiting, or suppressing cell adhesion" is not equivalent to a positive recitation of how to use the product for the treatment of a particular disease of real world relevance. The provisions of 35 USC 101 require that claimed subject matter be useful to be eligible for patentability. Case law has established that utility may not be based on mere assertion, but rather must be definite and in currently available form." *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966). Claims 12-14 are directed to mediating a biochemical pathway, thereby failing to set forth a definable utility. Unless the pathway at issue is critical to treating some condition, and the pathway modification and

disease treatment are inexorably linked, such pathway modification is devoid of utility. The Examiner suggests incorporating some of the specific diseases that Applicants are enabled for treating in the specification.

Conclusion

10. In conclusion, claims 1-7 and 9-15 are pending in the application, and claims 1-7 and 9-11 would be allowable if the non-elected subject matter is withdrawn, while claims 12-15 stand rejected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571.272.0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CEILA CHANG
PRIMARY EXAMINER
GROUP 1200 1625

Janet L. Coppins
July 22, 2004